



Systematic reviews of observational data



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“Epidemiologist know a lot about the correct way to conduct a research study but less about how to review and synthesize data from multiple studies and this, I suggest, is a principal source of the public’s confusion when faced with a new result from an epidemiological study”

Bracken MB. IJE 2001:954



What is a systematic review?

A review:

- ✓ clearly formulated question
- ✓ uses systematic and explicit methods to **identify** and **collect** relevant research
- ✓ uses systematic and explicit methods to **select**, **critically appraise** and **analyse** relevant research included.



What is a systematic review?

Statistical methods (meta-analysis)
may or may not be used to
summarise the results
of the included
studies





How much work is a systematic review?

~ 1139 hours

~ 30 person-weeks of full-time work

- ✓ 588 for protocol, searching and retrieval
- ✓ 144 for statistical analysis
- ✓ 206 for report writing
- ✓ 201 for administration

Source: Allen IE. JAMA, 1999;282:634



What are observational studies?

- ✓ Data from existing database
- ✓ Cross-sectional study
- ✓ Case series
- ✓ Case-control study
- ✓ Cohort study



RCT



Observational studies



Why do we need systematic reviews of observational studies?

- ✓ Test aetiological hypothesis
- ✓ Evaluation of interventions designed to prevent rare outcomes
- ✓ Evaluation if outcomes of interest are far in the future
- ✓ Evaluation of effectiveness in a community



MAOS are common

Type of article	Articles (n)
Meta-analysis of:	
Controlled trials	34
Observational studies	25
Methodological article	15
Traditional review	15
Other	11

Source: Egger M. Systematic reviews in Health Care. Meta-analysis in context. BMJ Books. 2001

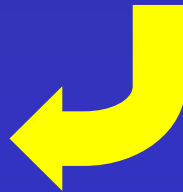


RCT

(Lack of precision)



Meta-analysis



More reliable estimates



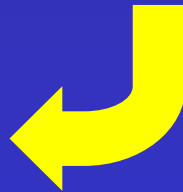


Observational studies

(Confounding, bias)



Meta-analysis



More reliable estimates????

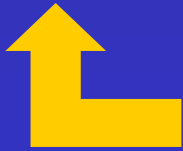


Confounding factors

Smoking



Suicide



Social/mental states



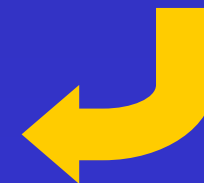
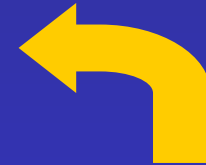
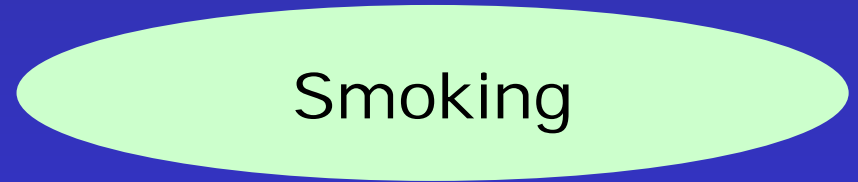


Confounding factors

Coffee consumption



Risk of myocardial infarction





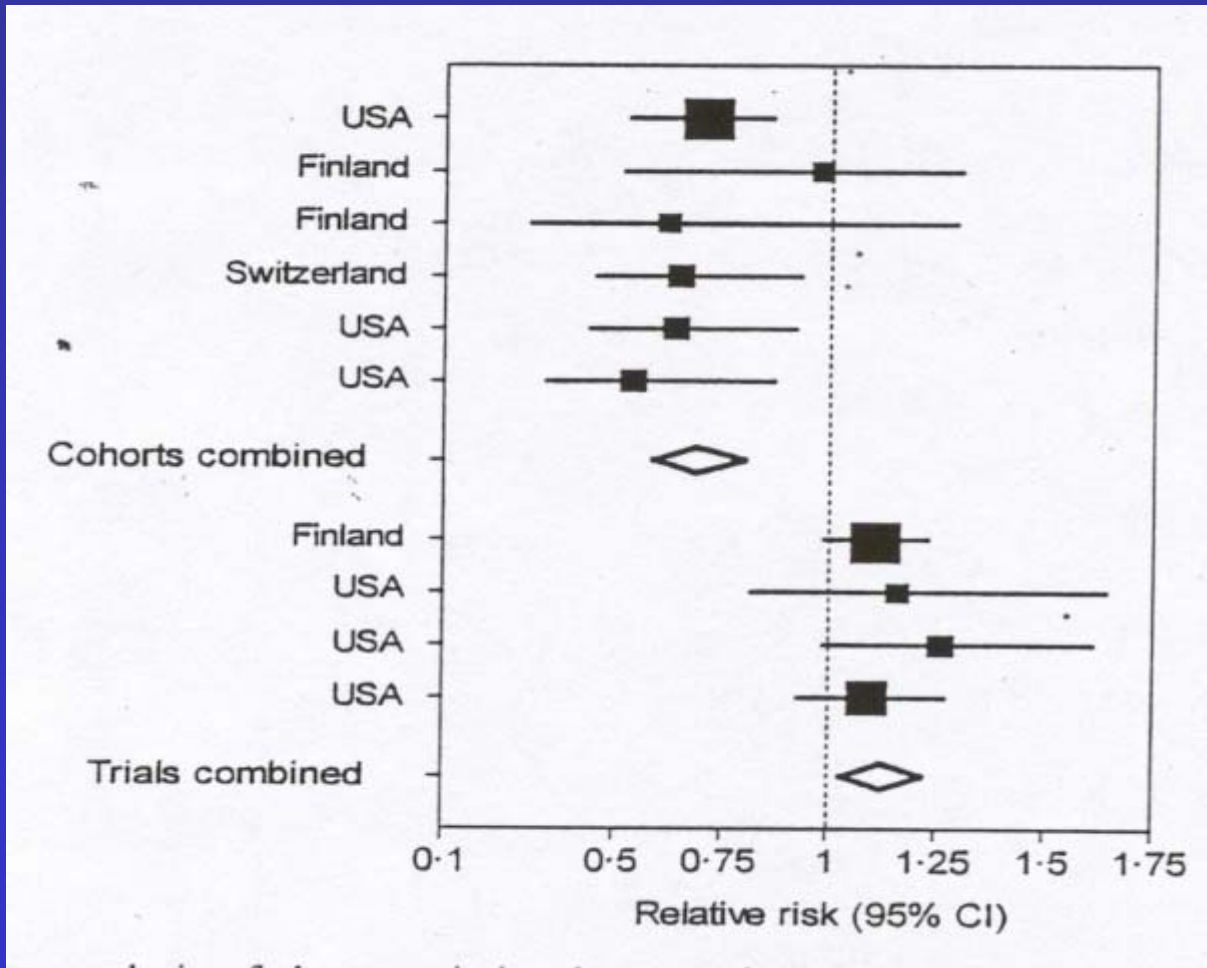
The protective effect of beta-carotene that wasn't

Cohorts

- Male health workers
- Social insurance, men
- Social insurance, women
- Male chemical workers
- Hyperlipidaemic men
- Nursing home residents

Trials

- Male smokers
- Skin cancer patients
- (Ex)-smokers, asbestos workers
- Male physicians





There are examples of observational studies producing similar results of those from RCT

But observational studies will always have to deal with bias and confounding because the intervention was deliberately chosen and not randomly allocated



Benson and Hartz, NEJM, 2000;342:1878-86

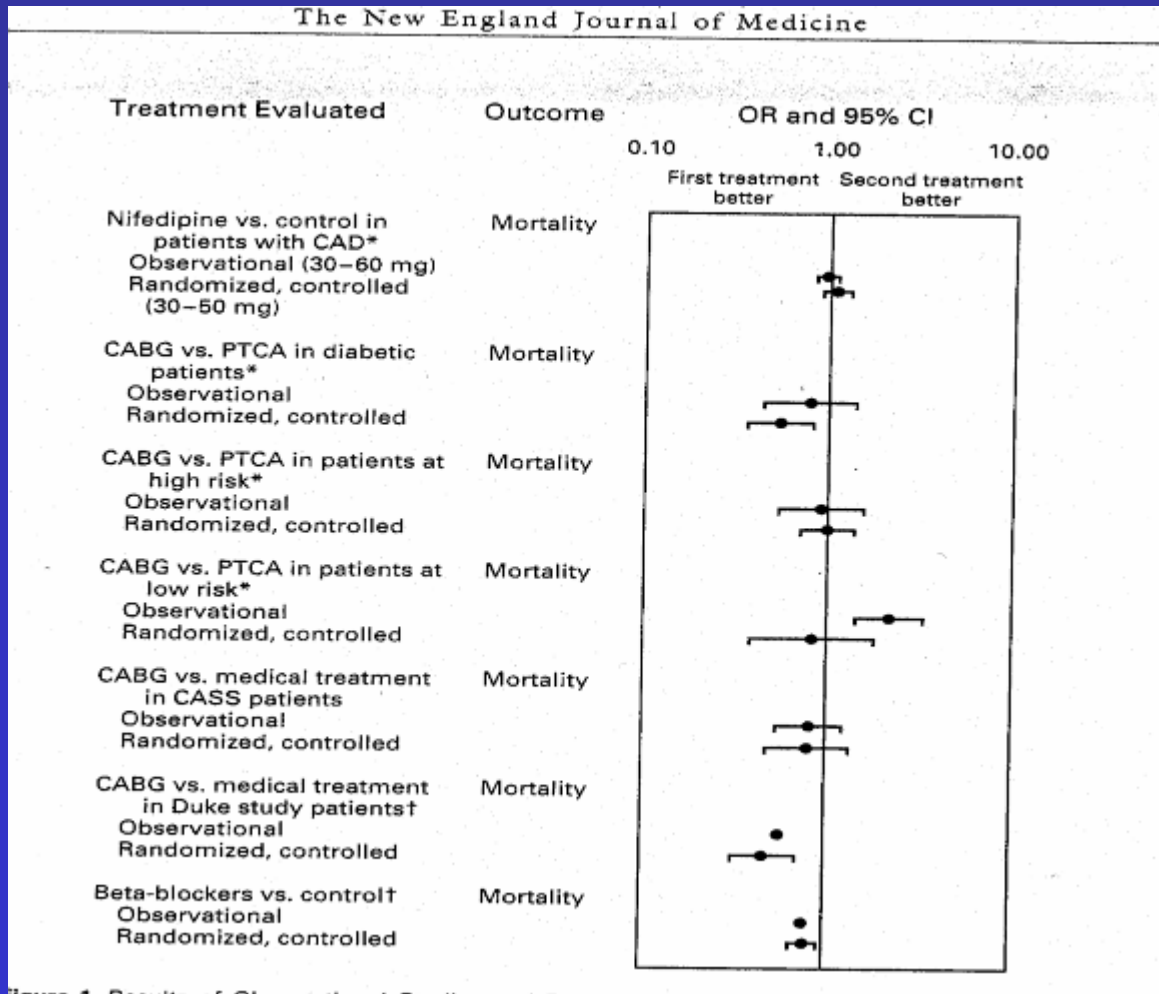
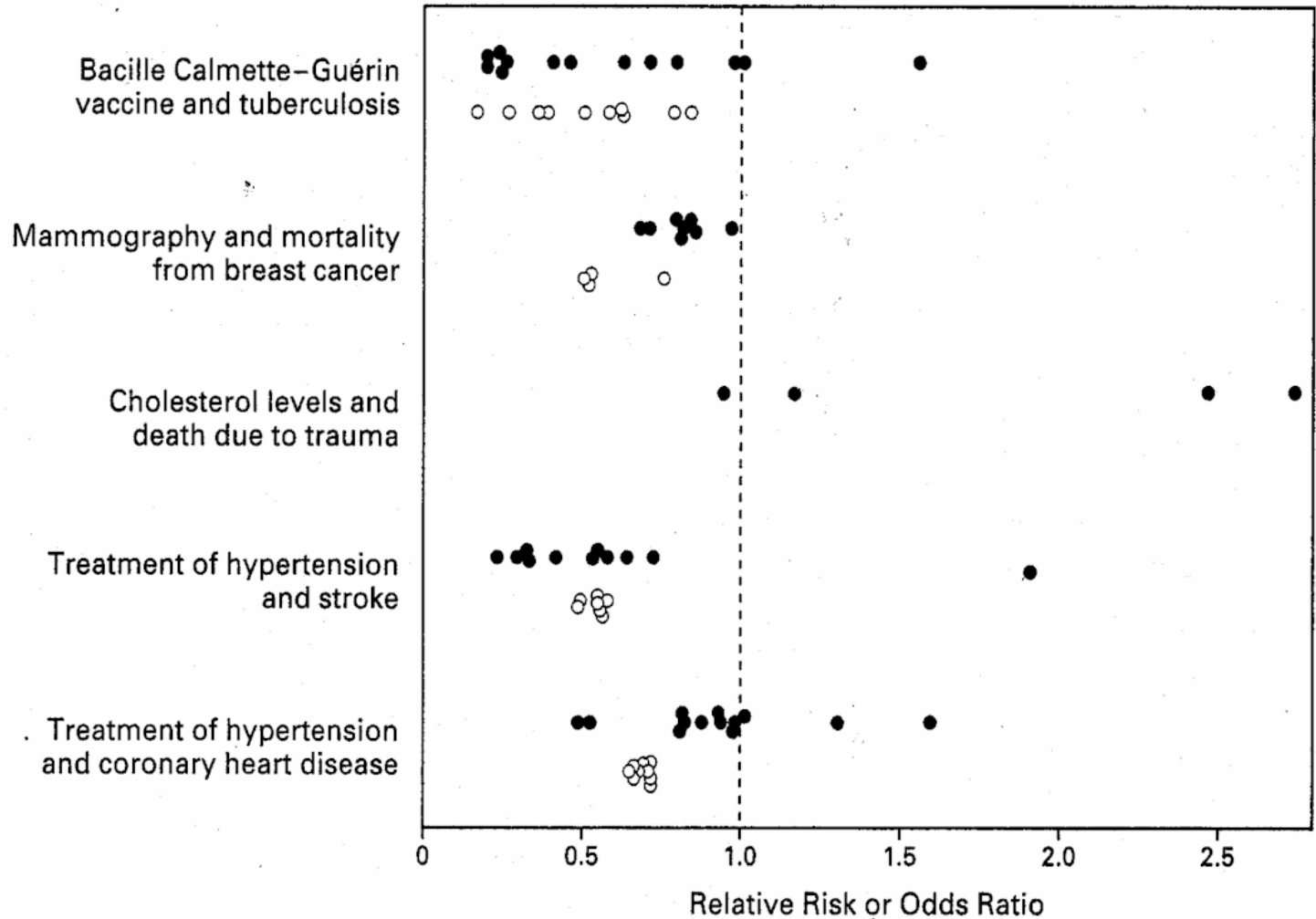
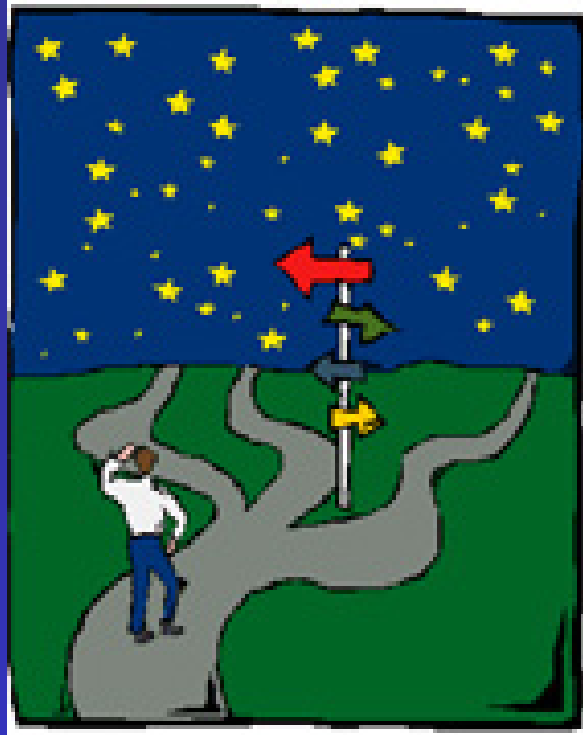


Figure 1. Results of Observational Studies and Randomized, Controlled Studies



Concato et al., NEJM, 2000;342:1887-92





This does not mean to return to narrative reviews



Benefits of MAOS:

- ✓ Systematic and explicit rules
- ✓ Statistical power
- ✓ Insight into variable interaction
- ✓ Detection of discrepancies
- ✓ Deepness into heterogeneity
- ✓ Identification of gaps in knowledge



Reporting of background should include:

- 1 Problem definition, hypothesis statement
- 2 Description of study outcome(s)
- 3 Type of exposure or intervention used
- 4 Type of study designs used
- 5 Study population



Reporting of search should include:

- 6** Qualifications of researchers
- 7** Search strategy including time period
- 8** Effort to include all available studies
- 9** Databases and registries searched
- 10** Searching software used
- 11** Use of hand searching
- 12** List of citations located and those excluded, including justification
- 13** Methods of addressing articles not published in English
- 14** Methods of handling abstracts and unpublished studies
- 15** Descriptions of any contact with authors



Reporting of methods should include:

- 16** Description of relevance/appropriateness of papers assembled for assessing the hypothesis to be tested
- 17** Rational for the selection and coding of data
- 18** Documentation about how data were classified and coded
- 19** Assessment of confounding
- 20** Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results
- 21** Assessment of heterogeneity
- 22** Description of statistical methods in sufficient detail to be replicated
- 23** Provision of appropriate tables and graphics



Reporting of results should include:

- 24** Graphic summarizing individual study estimates and overall estimate
- 25** Table giving descriptive information for each study included
- 26** Results of sensitivity testing (e.g. subgroup analysis)
- 27** Indication of statistical uncertainty of findings



Reporting of discussion should include:

- 28** Quantitative assessment of bias
- 29** Justification for exclusion
- 30** Assessment of quality of included studies



Reporting of conclusions should include:

- 31** Consideration of alternative explanations for observed results
- 32** Generalization of the conclusions
- 33** Guidelines for future research
- 34** Disclosure of funding source



Quality of reviews in Epidemiology

Breslow R. *AJPH*, 1998;88:475-7

All 1995 issues of 7 widely read epidemiology journals were searched for reviews



29 reviews were found



Reviews following quality guidelines

Guideline	Yes	Unable to determine	No
Search methods stated	6 (21)	1(3)	22(76)
Inclusion criteria reported	5(17)	4(14)	20(69)
Bias in selecting studies avoided	3(10)	26(90)	0(0)
Criteria for assessing validity reported	2(7)	15(52)	12(41)
Methods for combining findings reported	10(34)	6(21)	13(45)
Conclusions supported by data	24(83)	4(14)	1(3)



Search restriction: General medical journal, 2001

Search Procedure	19 meta-analyses	13 systematic reviews
Numerous Databases Searched (versus just MEDLINE)	13 (68%)	6 (46%)
Additional Searches Conducted (e.g., manual search of reference lists or textbooks)	17 (89%)	10 (77%)
Gray Literature Searched (e.g., manual search of conference or dissertation abstracts)	5 (26%)	4 (31%)
Contacted Experts to Find Unpublished Data	7 (37%)	2 (15%)
Cochrane Databases Searched	8 (42%)	4 (31%)
All Methods Employed	4 (21%)	1 (8%)

Source: Becker B, Morton S (see http://www.msri.org/calendar/talks/TalkInfo/1268/show_talk)



Search restriction: General medical journal, 2001

Language Restriction	19 meta-analyses	13 systematic reviews
None	6 (32%)	1 (8%)
English plus other lang.	2 (11%)	0 (0%)
English only	7 (37%)	7 (54%)
Unclear	4 (21%)	5 (38%)
Attempted to include unpublished studies	7 (37%)	5 (38%)

Source: Becker B, Morton S (see http://www.msri.org/calendar/talks/TalkInfo/1268/show_talk)



Other citations:

- ✓ Mulrow CD. The medical review article: state of the science. *Ann Intern Med* 1987, 6:233-240.
- ✓ McAlister FA, Clark HD, van Walraven C et al. The medical review article revisited: has the science improved? *Ann Intern Med* 1999, 131:947-951
- ✓ Bracken MB. Commentary: towards systematic reviews in epidemiology. *IJE* 2001, 30:954-957.



Summary

- ✓ SR and MA of observational studies are as common as reviews of RCT
- ✓ Confounding and selection bias often distort the findings
- ✓ Danger in producing very precise but spurious results
- ✓ More is gained by examining heterogeneity



WHO Systematic review of incidence/prevalence of maternal mortality and morbidity 1997-2002



Objectives

- To provide a comprehensive, standardised and reliable tabulation of available data on maternal morbidity
- To provide up-to-date data for future maternal mortality estimates
- To provide case-fatality rates



Search strategy

Electronic search

- Electronic databases (Medline, Embase, Popline, Cinahl, SocioFile, LILACS, CAB, Econlit, Biosis, PAIS)
- WHO on-line regional databases
- Internet searches (Google, web of science...)



Search strategy

Other searches

- Experts active in the field
- WHO regional offices
- Hand searching
- References lists
- Circulating documents



CHARACTERISTICS OF THE STUDY

3. Study design

- (1) Census
- (2) Cross-sectional
- (3) Cohort/longitudinal
- (4) Controlled trial
- (5) Incidence/Prevalence survey
- (6) Unknown

(7) Other, specify _____

<input type="checkbox"/>	<input type="checkbox"/>
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WHO CODE

4. Sampling

(1) Random sample

4a. Specify the method of randomization:

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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WHO CODE

(2) Non-random sample

4b. Specify the method of sampling:

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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WHO CODE

(3) Total population (i.e. census)

(4) Unknown

WHO systematic review

5. Data source

- (1) Vital statistics/census
- (2) Medical record
- (3) Special survey/interview
- (4) Multiple sources
- (5) Clinical data collected for the study
- (6) Other, specify _____

<input type="checkbox"/>	<input type="checkbox"/>
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WHO CODE

6. Lowest unit of data source

(1) Cluster

6a. Number of clusters

<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
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(2) Individual

(3) Other, specify _____

<input type="checkbox"/>	<input type="checkbox"/>
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WHO CODE



WHO systematic review

9. Population studied

- (1) Urban
- (2) Rural
- (3) Mixed
- (4) Unknown

10. Description of the characteristics of the population studied (e.g. socio-economic status, ethnic group, age group, etc.)

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WHO CODE



WHO systematic review

MATERNAL MORTALITY (cont.)			
26a. Cause distribution of maternal mortality			
Condition	(i) WHO code	(ii) No. of deaths	(iii) Percentage
26a.1) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>
26a.2) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>
26a.3) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>
26a.4) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>
26a.5) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>
26a.6) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>
26a.7) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>



WHO systematic review

32. Infections	WHO code
32a) Condition _____	<input type="text"/> <input type="text"/> <input type="text"/>
32b) Does the study include a definition?	Yes <input type="checkbox"/> No <input type="checkbox"/>
32c) If definition is included, please specify: _____ _____	<input type="text"/> <input type="text"/> <input type="text"/> WHO code
32d) Does the study explain the method of assessment of the infection?	Yes <input type="checkbox"/> No <input type="checkbox"/>
32e) If method of assessment is explained, please specify: _____ _____	<input type="text"/> <input type="text"/> <input type="text"/> WHO code



MATERNAL MORTALITY

25a. Maternal mortality estimates

i) Year

From		To	

ii) Age group

From		To	

iii) No. of deaths

--	--	--	--

iv)

Denominator							

v)

1. Live births
2. Pregnancies
3. Deliveries

--

vi)

MM Rate			

vii)

CI (95%)			

-

CI (95%)			

viii)

MM Ratio			

ix)

CI (95%)			

-

CI (95%)			

WHO systematic review



Citations identified
(Titles and/or abstracts)
64 586

Excluded
59 960

Full-text evaluation
(Articles and reports)
4626

Reasons for exclusion

- **92%** – no relevant data
- **6%** – sample size < 200
- **2%** – other reasons

Reasons for exclusion

- **57%** – no relevant data
- **15%** – sample size < 200
- **11%** – no dates reported
- **17%** – other reasons

Excluded
1988

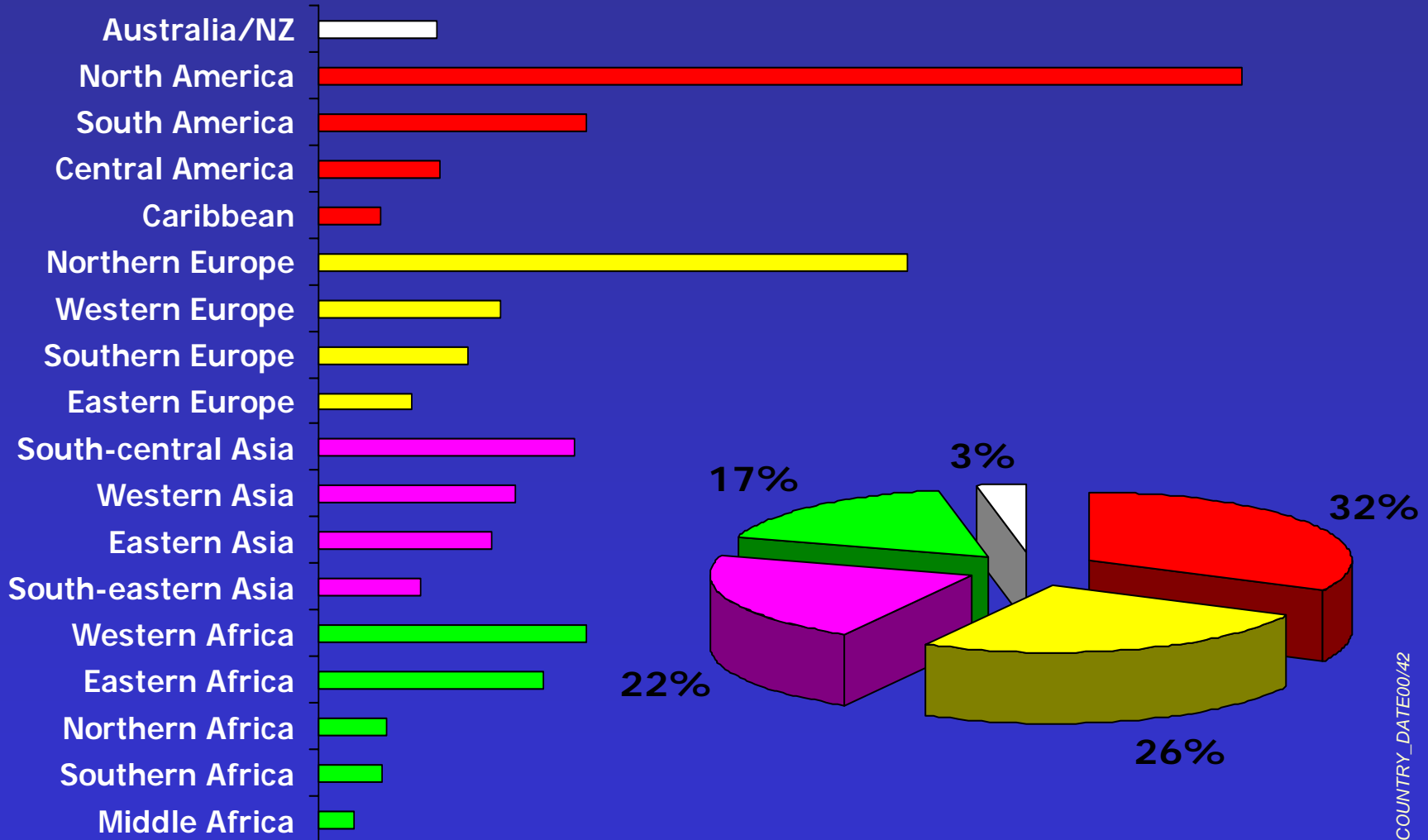
Included
2443

In process
195

Data processing complete
2204

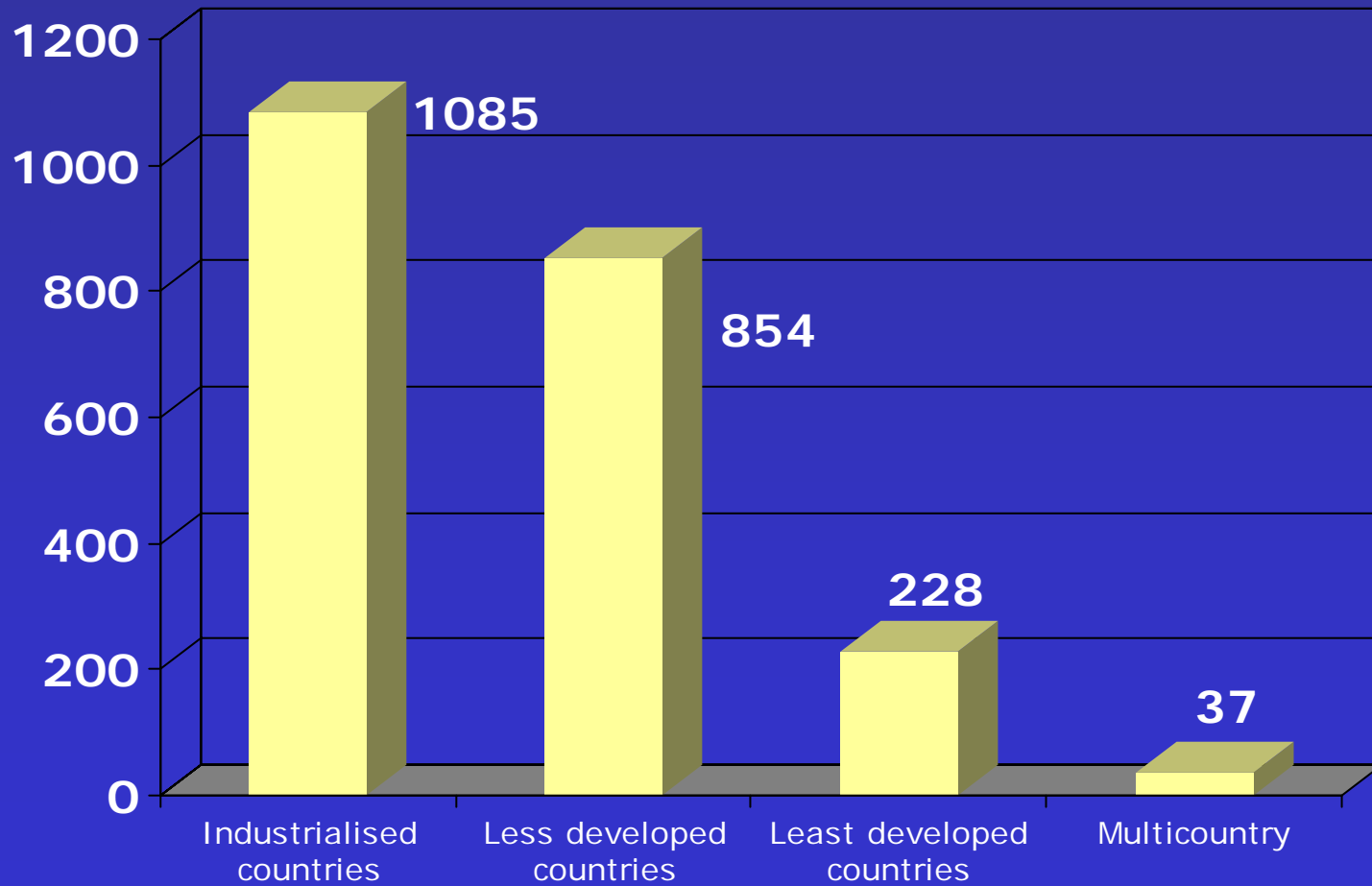


Regional distribution (n=2204)





Development status (n=2204)





Results: methodological quality of reported data

	Morbidity (n = 3215)	Mortality (n = 335)	Total (n = 3550)
High	103	8	111
Medium	1670	250	1920
Low	1442	77	1519



Reported morbidities (n=3215)

- ✓ Hypertensive disorders of pregnancy (16.3%)
- ✓ Haemorrhage (11.1%)
 - ✓ postpartum - 2.7%
 - ✓ antepartum / intrapartum - 2.2%
 - ✓ placenta praevia - 1.8%
 - ✓ abruptio placenta - 2.6%
 - ✓ other haemorrhage / unspecified - 1.8%
- ✓ Abortion (10.7%)
- ✓ Preterm delivery (8.3%)
- ✓ Stillbirth (6.3%)
- ✓ Diabetes in pregnancy (4.4%)
- ✓ Anaemia in pregnancy (4.3%)
- ✓ Ectopic pregnancy (3.0%)
- ✓ Perineal tears (2.6%)
- ✓ PROM (2.6%)
- ✓ Uterine rupture (2.1%)
- ✓ Postpartum sepsis (1.6%)
- ✓ Depression (1.9%)
- ✓ Obstructed labour (1.8%)



*"And it was so typically brilliant of you
to have invited an epidemiologist."*

